Regulus Receives Allowance from Japan and U.S. Patent Offices for HCV Intellectual Property, Expanding Leading Worldwide Patent Estate

- Japan Patent Office Joins Australian, European and U.S. Patent Offices in Granting Claims for Therapeutic Use of Inhibiting microRNA-122 for HCV Treatment

- U.S. Patent and Trademark Office Allows Claims for Therapeutic Use of anti-miR-122 in HCV Patients as Monotherapy or in Combination with Other Anti-Viral Therapies

LA JOLLA, Calif., April 23, 2012 /PRNewswire/ -- Regulus Therapeutics Inc., a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, today announced that the Japan Patent Office has issued a Decision to Grant a Patent in the 'Sarnow' patent series for microRNA-122 (miR-122) therapy in the treatment of chronic hepatitis C virus (HCV) infection. The Sarnow patent estate, owned by Stanford University and exclusively licensed to Regulus, has already produced patents in Australia, Europe and the United States, and covers the use of a broad class of anti-miR inhibitors of miR-122 for the treatment of HCV.

Regulus also announced today that the U.S. Patent and Trademark Office has allowed claims in a third Sarnow patent application, relating to the use of anti-miR-122 agents as monotherapy or in combination with other anti-viral therapies, to treat HCV-infected patients.

"The recent allowance of miR-122 therapy claims further broadens Regulus' dominant and comprehensive intellectual property estate covering microRNA therapeutics," said Kleanthis G. Xanthopoulos, Ph.D., President and CEO of Regulus Therapeutics Inc. "The HCV landscape continues to be a dynamic and ever-evolving space, with improvements upon direct-acting antiviral therapy on the horizon. We believe anti-miR-122 is attractively positioned for use in combination with direct-acting antivirals to further reduce viral load and suppress viral resistance."

Regulus' Patent Estate for Anti-miR-122 Therapeutic Agents

Regulus controls a comprehensive and dominant patent estate related to microRNA therapeutics, including anti-miR-122 therapeutic agents. Specifically for miR-122, Regulus controls the following:

- The 'Sarnow' patent estate claiming the use of an anti-miR-122 to treat HCV, as a single therapeutic agent or in combination with other HCV therapeutic agents (including US Patent No. 7,307,067; US Patent No. 7,838,504; EP Patent No. 1 747 023; and recently accepted Australian Patent Application No. 2005240118; recently allowed US Application No. 12/950,672, and recently allowed Japan Application No. 2007-511489);
- The 'Esau' patent claiming the use of anti-miRs targeting miR-122 as inhibitory agents (US Patent No. 7,683,036);
- The 'Tuschl III' patent claiming compositions of matter for miR-122 and complementary oligonucleotides (US Patent No. 7,232,806);
- The 'Manoharan' patent claiming antagomirs, including antagomirs targeting miR-122 (US Patent No. 7,582,744); and
- A Regulus-owned European patent claiming the use of miR-122 antagonists for reducing cholesterol (EP 1 931 782 and Australian Patent No. 2006284855).

miR-122 is a liver-expressed microRNA that has been shown to be a critical endogenous "host factor" for the replication of HCV, and anti-miRs targeting miR-122 have been shown to block HCV infection (Jopling *et al.* (2005) *Science* 309, 1577-81).

In addition to Regulus' attention to hepatitis C, the Company is advancing multiple other microRNA therapeutic programs toward the clinic in the areas of oncology, immune-inflammatory diseases, fibrosis and metabolic diseases.

About microRNAs

The discovery of microRNA in humans during the last decade is one of the most exciting scientific breakthroughs in recent history. microRNAs are small RNA molecules, typically 20 to 25 nucleotides in length, that do not encode proteins but instead regulate gene expression. More than 700 microRNAs have been identified in the human genome, and over one-third of all human genes are believed to be regulated by microRNAs. A single microRNA can regulate entire networks of genes. As such, these molecules are considered master regulators of the human genome. microRNAs have been shown to play an integral role in numerous biological processes, including the immune response, cell-cycle control, metabolism, viral replication, stem cell differentiation and human development. Most microRNAs are conserved across multiple species, indicating the evolutionary importance of these molecules as modulators of critical biological pathways. Indeed, microRNA

expression, or function, has been shown to be significantly altered in many disease states, including cancer, heart failure and viral infections. Targeting microRNAs with anti-miRs, antisense oligonucleotide inhibitors of microRNAs, or miR-mimics, double-stranded oligonucleotides to replace microRNA function opens potential for a novel class of therapeutics and offers a unique approach to treating disease by modulating entire biological pathways.

About Regulus Therapeutics Inc.

Regulus Therapeutics is a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs. Regulus is using a mature therapeutic platform based on technology that has been developed over 20 years and tested in more than 5,000 humans. The company works with a broad network of academic collaborators and leverages the oligonucleotide drug discovery and development expertise of its founding companies, Alnylam Pharmaceuticals (*NASDAQ:ALNY*) and Isis Pharmaceuticals (*NASDAQ:ISIS*). Regulus is advancing microRNA therapeutics toward clinical development in several areas, including fibrosis, hepatitis C, immuno-inflammatory diseases, metabolic diseases and oncology. Regulus' intellectual property estate contains both the fundamental and core patents in the field and includes over 600 patents and more than 300 pending patent applications pertaining primarily to chemical modifications of oligonucleotides targeting microRNAs for therapeutic applications. In April 2008, Regulus formed a major alliance with GlaxoSmithKline to discover and develop microRNA therapeutics for immuno-inflammatory diseases. In February 2010, Regulus and GlaxoSmithKline entered into a new collaboration to develop and commercialize microRNA therapeutics targeting microRNA-122 for the treatment of hepatitis C infection. In June 2010, Regulus and sanofi-aventis entered into the largest-to-date strategic alliance for the development of microRNA therapeutics with an initial focus on fibrosis.

For more information, please visit http://www.regulusrx.com. Regulus is also on YouTube at http://www.youtube.com/user/RegulusRx#p/f and on Twitter at www.twitter.com/regulusrx .

Forward-Looking Statements

This press release includes forward-looking statements regarding the future therapeutic and commercial potential of Isis', Alnylam's and Regulus' business plans, technologies and intellectual property related to microRNA therapeutics being discovered and developed by Regulus, including statements regarding the therapeutic potential of targeting miR-122 for treating chronic hepatitis C virus infection. Any statement describing Isis', Alnylam's or Regulus' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. Such parties' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause their results to differ materially from those expressed or implied by such forward-looking statements. Although these forward-looking statements reflect the good faith judgment of the management of each such party, these statements are based only on facts and factors currently known by Isis, Alnylam or Regulus, as the case may be. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Regulus', Alnylam's, and Isis' programs are described in additional detail in Alnylam's and Isis' annual reports on Form 10-K for the year ended December 31, 2011. Copies of these and other documents are available from Alnylam or Isis.

SOURCE Regulus Therapeutics Inc.

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